reactions between oxygen and foodstuffs would not occur under ordinary atmospheric conditions and that enzymes must be responsible. The Thunberg-Knoop-Wieland model emphasized reactions in which enzymes operated on a substrate to release hydrogen atoms (which would then combine with molecular oxygen, were it available). The other model, developed by Otto Heinrich Warburg, construed the enzyme (ferment by his terminology) as operating on oxygen, which would then combine with hydrogen from the substrate.

Heinrich Otto Wieland was an organic chemist who began his exploration of oxidation using inorganic catalysts such as palladium black. He found that when no oxygen was present, the catalyst would operate for a short time before it became saturated with hydrogen. He proposed that when oxygen was available, it served only to receive the hydrogen removed from the substrate. He substantiated this proposal by showing that methylene blue, a synthetic dye that is readily reduced to leuco-methylene blue, could substitute for oxygen in maintaining the reaction (Wieland, 1913). He proposed the following schema for oxidation of a compound RH_2 to R (Pd designates palladium, the catalyst, and Mb methylene blue, the dye):

$$RH_2 + Pd \rightarrow R + PdH_2$$

$$PdH_2 + Mb \rightarrow Pd + MbH_2.$$

When a substrate such as an aldehyde (RCHO) lacked two removable hydrogen atoms, he proposed that it was first hydrated (a water molecule was added) and then two hydrogen atoms were removed:

$$RCHO + H_2O \rightarrow RCH(OH)_2 \rightarrow RCOOH + H_2.$$

Wieland's scheme established a new conceptualization of oxidation as dehydrogenation – the removal of hydrogen rather than the addition of oxygen – and of its relation to reduction. Since the hydrogen released by the substance being oxidized had to be accepted by another substance that was thereby reduced, he proposed that these reactions were necessarily coupled as "two expressions of one process of dehydrogenation" (p. 3340). Wieland then extended this account to biological oxidation. He proposed that oxygen, when present, was the substance reduced in cells, yielding hydrogen peroxide (H_2O_2) that the enzyme catalase would quickly convert to water. Importantly, he showed that when oxygen was not present, oxidation could still occur in biological entities. Specifically, ethanol and acetaldehyde could be oxidized to acetic acid in bacteria if methylene blue was available as a hydrogen acceptor.